

BOVINE MASTITIS: GLOBAL QUANDARY “A REVIEW”

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ABSTRACT

Mastitis is one of the oldest and the commonest disease probably as long as mankind has milked cows. Mastitis is a complex disease which occurs in many forms namely acute, gangrenous, chronic, clinical and subclinical characterized by inflammation of bovine udder and huge milk loss. It is among the topmost disease in view of causing economic loss to the farmers as well as the country. Apart from that indiscriminate use of antibacterial drugs in field to treat the disease leads to serious consequences like anti-microbial resistance. In more recent times concerns have been raised that the use of antimicrobials has caused resistance in bacteria isolated from treated animals, other animals in the population and from food derived from animals for human consumption. It is of serious concern. The present review is in context to this address in general about mastitis and the role of molecular assisted selection (MAS) in overcoming this giant problem.

KEYWORDS: Mastitis, Antibacterial, Antimicrobial & MAS

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INTRODUCTION

India possesses world's largest bovine population which is about 14.7% of the world cattle population. The total cattle population is 190.90 million out of which indigenous cattle population is 151.17 millions and exotic/crossbred cattle population is 39.73 millions (Anonymous, 2012). India has 108.7 million buffalo population and they comprise approximately 56% of the total world's buffalo population. The total indigenous cattle population decreased by 8.94% and crossbred population increased by 20.18% compared to 18th Livestock Census. At present, the total milk production in India is 146.3 million tonnes. A large population of indigenous cattle (151.17 million) contributes only 20 % (29.26 million tonnes) compared to a small population of crossbreds/exotic (39.73 million) contributing 25 % (36.5 million tonnes) to total milk production in the country. The increased production of milk has improved the per capita availability to 322g/day but it still remains half the world average. The major concern of country is the low productivity of indigenous animals and huge dairy losses due to production related diseases in high yielding cattle.

In today's world, where agricultural land is reducing day by day an increase in global population coupled with the increasing demands for milk as an economic food and as an industrial raw food product has necessitated an increase in production by dairy farmers. Consumption of dairy products has also increased at similar levels with a sharper increase in recent years, primarily due to a larger personal income base for individuals (Mantovaniet al., 2002). To cope up with the growing demand of milk and milk products due to ever increasing human population of

our country, it becomes imperative to increase the production potential of our indigenous livestock especially the cattle & buffalo. Among the several bottlenecks in achieving the milk production targets, occurrence of diseases continues to remain the most challenging impediment.

ECONOMIC LOSSES DUE TO MASTITIS

The Indian dairy sector is facing nearly Rs. 60,000 million annual losses due to mastitis, out of which Rs. 4,4000 million is due to sub clinical mastitis which is more than clinical mastitis (Rs.1,6000 million) (Burman,2014). In a commercial milking environment, dairy cattle need to be in perfect physical condition to maintain a high level of milk production. The risk of lesions and infections that develop in modern dairy farming has consequently increased. Low milk production has been attributed to a large extent to the control of diseases in dairy cattle, of which mastitis accounts for the largest economic losses on dairy farms in many countries in the world, including the USA, United Kingdom, Europe, Australia and South Africa (Petrovski *et al.*, 2006). This disease costs the US dairy industry about 1.7 to 2 billion USD each year (Jones *et al.*, 2010). Improving udder health and decreasing the incidence of udder infection and inflammation in dairy herds, will result in increased milk production as huge losses are directly or indirectly incurred through loss of milk during treatment periods, culling of cows and death of clinically infected cattle. Mastitis control programmes addressing various aspects of dairy farming such as feeding practices, animal husbandry, hygiene and general health care can contribute towards reducing the incidence of udder infections. Treating infection with antimicrobials can, in conjunction with good farming practices assist in this endeavour to eliminate, or at least decrease, the incidence of mastitis infection within a dairy herd.

Table: Mastitis: Causative Agent

Sr. No.	Causative Agent
1.	<i>Pseudomonas aeruginosa</i>
2.	<i>Staphylococcus aureus</i>
3.	<i>Staphylococcus epidermidis</i>
4.	<i>Streptococcus agalactiae</i>
5.	<i>Streptococcus uberis</i>
6.	<i>Brucella melitensis</i>
7.	<i>Corynebacterium bovis</i>
8.	<i>Mycoplasma</i> spp.
9.	<i>Escherichia coli</i> (<i>E. coli</i>)
10.	<i>Klebsiella pneumoniae</i>
11.	<i>Klebsiella oxytoca</i>
12.	<i>Enterobacter aerogenes</i>
13.	<i>Pasteurella</i> spp
14.	<i>Trueperella pyogenes</i> (previously <i>Arcanobacterium pyogenes</i>)
15.	<i>Proteus</i> spp.
16.	<i>Prototheca zopfii</i> (achlorophyllic algae)
17.	<i>Prototheca wickerhamii</i> (achlorophyllic algae)

Anonymous, 2017

Mastitis, the inflammation of parenchyma of mammary glands is a complex multi etiological disease affecting dairy animals. “Mastitis” describes an inflammatory reaction in the mammary gland. The term comes from the Greek derived word elements *masto-* referring to the mammary gland and *-itis* meaning – “inflammation” (Blood and Studdert, 1999). Although “mastitis” could technically be used to describe any udder injury that may result in inflammation, it is generally accepted that the causative agents for the inflammatory reaction are microorganisms that have gained entry into

the teat canal and mammary tissue. The extent of the infection that occurs as microorganisms multiply and proliferate within the mammary tissue determines the type of mastitis affecting the cow udder. Bovine mastitis is a disease complex which occurs in acute, gangrenous, chronic, and subclinical forms of inflammation of the bovine udder, and is due to a variety of infectious agents; animal care, hygiene, and management are important factors in this dairy cow disease of great economic importance. Mastitis continues to be the most costly disease of dairy animals. Clinical mastitis is characterized by sudden onset, swelling and redness of the udder, pain and reduced and altered milk secretion from the affected quarters. The milk may have clots, flakes or of watery consistency and accompanied by fever, depression and anorexia. The subclinical mastitis is characterized by having no visible signs either in the udder or in the milk, but the milk production decreases and the Somatic cell count (SCC) increases, having greater impact in older lactating animals than in first lactation heifers. A negative relationship generally exists between SCC and the milk yield (Khan and Khan, 2006). Milk from normal uninfected quarters generally contain below 200,000 somatic cells /ml. A value of SCC above 300,000 is abnormal and an indication of inflammation in the udder. There is a plethora of evidence that the dairy cow milk has a natural level of 100,000-150,000 somatic cells/ml and higher SCC indicates secretory disturbance (Hillerton, 1999).

EFFECT ON MILK PARAMETERS

Mastitis impairs the quality of milk and milk products (Philpot, 2003). Mastitis can cause a decline in potassium and lactoferrin. It also results in decreased casein, the major protein in milk. As most calcium in milk is associated with casein, the disruption of casein synthesis contributes to lowered calcium in milk. The milk protein continues to undergo further deterioration during processing and storage. Milk from cows with mastitis also has a higher somatic cell count (Kandasamy *et al.* (2011). Generally speaking, the higher the somatic cell count, the lower the milk quality. Field surveys of major livestock diseases have ranked mastitis as number one disease of dairy animals (Khan and Khan, 2006). Management strategies involve the extensive use of antibiotics to treat and prevent this disease. Prophylactic dosages of antibiotics used in mastitis control programmes could select for strains with resistance to antibiotics. In addition, a strong drive towards reducing antibiotic residues in animal food products has led to research in finding alternative antimicrobial agents.

MARKER BASED SELECTION METHODOLOGY FOR MASTITIS RESISTANCE

In India, sub clinical mastitis (varying from 10-50% in cows and 5-20% in buffaloes) is more important than clinical mastitis (1- 10%) (Awale *et al.*, 2012). Control strategies against mastitis mainly rely upon antibiotic therapy, vaccination and farm management practices to limit the duration of infection and to contain infectious spread of pathogens. But these methods had little success in controlling mastitis. Genetic selection for increased milk yield and improved composition had resulted in increased susceptibility to mastitis (Heringstad *et al.*, 2003). In order to rectify this unwanted drift, genetic improvement through selection for resistance against mastitis was explored for dairy cows primarily, then for dairy ewes and goats (Rupp and Boichard, 2003). A fair amount of genetic research related to udder health has already been performed due to its importance from economic as well as from quality control point of view (Ogorevc *et al.*, 2009; Schrooten *et al.*, 2000; Ashwell *et al.*, 1997). Release of cattle genome sequence in public domain has led to the discovery of new markers and creation of synteny maps including data from other species.

Also it is generally accepted that undesirable genetic relationships exist between production and mastitis (Emanuelson *et al.*, 1988; Heringstad *et al.*, 2005; Hansen *et al.*, 2002). Hence there is a need to develop sustainable

breeding strategies to reduce incidence of mastitis and also to improve the quality of milk production (Bagheri *et al.*, 2013). Conventionally selective breeding is a main focus to improve the genetics of animals. This includes progeny testing and various selection programs. Assisted reproductive technologies such as artificial insemination, multiple ovulation, and embryo transfer have been applied and there has been a dramatic improvement in the productivity of animals from the selective breeding of animals. (Lindhe *et al.* 2008, Sartori *et al.* 2006, Singh *et al.* 2006, Singh *et al.* 2007, Singh *et al.* 2008, Kumar *et al.* 2009, Kumar *et al.* 2008, Singh *et al.* 2010).

However, traditional breeding techniques in dairy cattle take many years and do not efficiently take into account all sources of genetic variability. Similarly, in sex-limited, low heritable, or late-expressed traits, the impact of traditional breeding is limited. The use of molecular markers will help to address the problems associated with traditional selection and thus help to select genetically superior animals. For better productivity and disease resistance, molecular markers have contributed much (Singh *et al.* 2013).

A selection strategy by improving the host genetics through genetic marker selective breeding has now been practiced widely (Wang *et al.*, 2011). Genomic selection utilizes molecular high density single nucleotide polymorphism (SNP) markers (Meuwissen *et al.*, 2001). A suitable control strategy can be devised only if we understand the host genetics and judicious application of the newer technologies like genomic selection to plan better breeding policies that will incorporate traits like mastitis tolerance. In India, the dairy breeding programmes are directed solely for high milk production and no emphasis has been given to mastitis resistance. Indirect selection based on somatic cell count and candidate gene markers can help to increase the efficiency of such breeding programmes.

In the last decade, many fine mapping experiments have resulted in identification of several QTLs in cattle. These QTLs cover large chromosomal regions involving hundreds or thousands of genes. Several chromosomal regions have been linked to marked effects on mastitis resistance. However, beyond fine mapping, the ultimate target of QTL analysis is the identification of causal gene itself which facilitate identification of resistance genes and alleles (Reinard and Riollot, 2005). Ogorevc *et al.*, (2009) developed a database on different candidate gene loci in mammary gland development, milk production and resistance or susceptibility to mastitis. Functional traits of the mammary gland have been studied using different approaches, including the QTL approach, association studies and the candidate gene approach. Nevertheless, breeding goals of many countries has been diversified to include health and functional traits in an effort to minimize and reverse the decline in these health traits (Miglior *et al.*, 2005).

There is considerable evidence that resistance to infectious diseases have genetic basis (Bishop and Mackenzie, 2003), therefore, attention needs to be focused on the genes responsible for disease resistance, in particular to mastitis in dairy animals. Overall, an identification of biomarkers for mastitis resistance will not only help to select the healthier animals, but will also be useful for understanding the changes associated with disease resistance at the genomic, proteomic and metabolic levels.

CANDIDATE GENES ASSOCIATED WITH MASTITIS RESISTANCE

There are a number of candidate genes like major histocompatibility complexes (MHC), interleukins (IL), toll like receptors (TLR), lactoferrin, CARD15, FEZL, CD14, complement component 4 (C4A), Mannose Binding Lectins (MBL1 and MBL2) etc. which are associated with resistance against mastitis. (Rupp and Boichard, 2003; Wang *et al.*, 2012; Zhao *et al.*, 2012). (Table 1)

Table 1: Association of Candidate Gene Polymorphism with Mastitis in Dairy Cattle

Gene	Reference
BoLA-DRB3	Sharif <i>et al.</i> , 1998; Nascimento <i>et al.</i> , 2006; Rupp <i>et al.</i> , 2007
CXCR2	Youngerman <i>et al.</i> , 2004
FEZ	Sugimoto <i>et al.</i> , 2006
Lactoferrin	Wojdak-Makysmiec <i>et al.</i> , 2006
TLR4	Sharma <i>et al.</i> , 2006; Wang <i>et al.</i> , 2007; Wang <i>et al.</i> , 2008
CYP11B1	Kaupeet <i>et al.</i> , 2007
CCL2, IL8	Leyva-Baca <i>et al.</i> , 2007
CARD-15	Pant <i>et al.</i> , 2007
CXCR1	Leyva-Baca <i>et al.</i> , 2008
S100A8	Ogorevc <i>et al.</i> , 2008; Ogorevc <i>et al.</i> , 2009
CD14	Ibeagha <i>et al.</i> , 2008; Beecher <i>et al.</i> , 2010
BRCA1	Yuan <i>et al.</i> , 2012
MBL1	Wang <i>et al.</i> , 2011 ; Liu <i>et al.</i> , 2011; Yuan <i>et al.</i> , 2013, Asaf <i>et al.</i> , 2014a and 2014b
MBL2	Wang <i>et al.</i> , 2012 ; Zhao <i>et al.</i> , 2012
C4A	Yang <i>et al.</i> , 2012a; Yang <i>et al.</i> , 2012b

CONCLUSIONS

In order to cope up with the increasing population and decreasing agriculture land scenario there is an urgency to frame the breeding policies of cattle keeping in mind this multi etiological disease. Selection of disease resistance animals well adapted to the agro-climatic conditions is the need of the hour and to achieve this MAS (Marker assisted selection) should be practiced so that the mastitis resistant animals can be selected and further bred. Such improvements will not only increase profitability of the farmers, but also leads to open an era of organic livestock dairy farming that is very beneficial for human health.

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